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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/311,996	05/14/1999	EUGENI A. VAISBERG	19681-4	1991

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EXAMINER

BRUSCA, JOHN S

ART UNIT PAPER NUMBER

1631

DATE MAILED: 03/10/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/311,996	VAISBERG ET AL.	
	Examiner	Art Unit	
	John S. Brusca	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 49-57, 60, 61 and 63-66 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 49-57, 60, 61 and 63-66 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 11 January 2002 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|--|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>12/30/2004</u> . | 6) <input type="checkbox"/> Other: ____ |

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DETAILED ACTION

Terminal Disclaimer

1. The terminal disclaimers filed on 30 December 2004 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of Application Numbers 09/718685 and 09/310879 has been reviewed and is accepted. The terminal disclaimer has been recorded.
2. In the future the applicants may wish to file a single terminal disclaimer that disclaims multiple applications and/or patents to avoid paying multiple terminal disclaimer fees.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 49-57, 60, 61, and 63-66 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to:

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1) a computer program that executes a method of cell image analysis that includes a step reciting “wherein some of said features from a first cell type are combined with features from a second cell type to yield one or more composite descriptors” in claims 49-55 and 66;

2) a computer program that executes a method of cell image analysis that includes a step reciting “wherein some of said features from a first type are combined with features from a second cell type to yield one or more composite features” in claims 56, 57, 60, and 61; and

3) a computer program that executes a method of cell image analysis that includes a step reciting “wherein at least some of said descriptors combine features from cells of different cell types” in claims 63-65.

The specification does not describe composite descriptors or descriptors which comprise features of different cell types.

5. Applicant's arguments filed 30 December 2004 have been fully considered but they are not persuasive. The applicants point to a number of passages in the specification in support of written description of composite descriptors, most notably at page 24, lines 17-19. The applicants further state that some of the support is generic to composite descriptors. However none of the pointed to passages explicitly describes the claimed species of descriptor that is a composite descriptor comprising features of two different cell types.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

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(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

7. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 49-57, 60, 61, and 63-65 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pauwels et al. (Journal of Pharmacological and Toxicological Methods, Vol.

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37, pages 105-115 (1997), cited as reference AE in the Information Disclosure Statement filed 14 May 1999) in view of Paull et al. (newly cited in this Office action).

The claims are drawn to a computer program on media that executes a cell image analysis method comprising steps of receiving images of components of a plurality of cells of different types that have been manipulated, producing composite descriptors that include information from cells of different types, and use of principal component analysis to produce a fingerprint of the effect of the manipulation on the different cell types. In some embodiments the components of the cells are organelles or nucleic acids, the manipulation is application of a chemical compound such as a drug, the information collected is relevant to toxicity or metabolism. In some embodiments the program predicts properties of a compound based on its effect on cells.

Pauwels et al. shows in the abstract and throughout a method of analyzing the effect of a variety of antitumor drugs on tumor cell lines by analysis of digital images of treated cells. Three cell lines and thirty drugs were examined. On page 107, Pauwels et al. details the computer mediated image analysis of the cells. Pauwels et al. determines 15 of parameters of the cells and derive data for the cells including nuclear area, DNA content, and chromatin texture. Pauwels et al. shows in figures 3-6 the results of principal component analysis for the drugs for each cell line. In figure 6 Pauwels et al. show that the analysis shows that classes of drugs with common features and modes of action can be determined by formation of centroids in the analysis. Pauwels et al. concludes on pages 112-114 that their method can be used to assign drugs to classes of drugs on the basis of the effects of the drugs on treated cells as determined by their

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image analysis method. Pauwels et al. does not show descriptors or fingerprints that comprise information of a plurality of cell lines.

Paull et al. shows a computer program called COMPARE that analyzes the effect of antitumor drugs on a panel of 60 different tumor cell lines. The information obtained from the cell lines was growth inhibition. Paull et al. show on page 1089 that their method produces fingerprints for each drug tested that show a structure-function relationship. Paull et al. calculates statistical measures of growth inhibition that considers the effect of a drug on all cell lines tested in pages 1089-1091, and the data are summarized in Table 2. Paull et al. conclude that drugs with similar modes of action cluster with similar values on page 1092.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to write a computer program to perform the method of Pauwels et al. because Pauwels et al. shows use of algorithms to analyze cell image data and Paull et al. shows a computer program that performs similar analysis of drug treated tumor cell lines. It would have been further obvious to modify the program of Pauwels et al. by construction of descriptors or fingerprints derived from the plurality of tumor cell lines tested by Pauwels et al. because Paull et al. shows that consideration of data from a plurality of tumor cell lines allows for drugs to be clustered by mode of action or structure while considering their effects on a wide range of tumor cell types.

10. Claims 63 and 66 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pauwels et al. in view of Paull et al. as applied to claims 49-57, 60, 61, and 63-65 above, and further in view of Rojanasakul (cited in the Office action mailed 10 March 2003).

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The claims are drawn to a computer program on media that executes a cell image analysis method comprising steps of receiving images of components of a plurality of cells of different types that have been manipulated by application of an antisense polynucleotide, producing descriptors that include information from cells of different types, and predicting properties of a compound based on its effect on cells.

Pauwels et al. in view of Paull et al. as applied to claims 49-57, 60, 61, and 63-65 above, does not show application of antisense oligonucleotides to cells.

Rohanasakul shows in the abstract and throughout that antisense oligonucleotides can be used to modulate gene expression and has potential to be used as a therapeutic for human diseases.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify the program of Pauwels et al. in view of Paull et al. as applied to claims 49-57, 60, 61, and 63-65 above by use of cells treated with antisense oligonucleotides because Rohanasakul shows that antisense oligonucleotides have potential as therapeutic drugs and manipulation of cells with antisense oligonucleotides allows for study of their effects on cell lines and for comparison with the effects of other drugs.

11. Applicant's arguments filed 30 December 2004 have been fully considered but they are not persuasive. The applicants state that Pauwels et al. at page 109, lines 10-15 teaches away from using the method of Paull et al. However a review of the references does not support the applicant's characterization of the teachings of Pauwels et al. Pauwels et al. initially screened one cell line treated with alternate drugs in figure 2 for a single parameter, DNA content.

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Pauwels et al. concluded that different classes of drugs could not be distinguished by the method shown in figure 2. Pauwels et al. then proceeded to utilize a multivariate analysis in which a single cell line was treated with alternative drugs and analyzed for multiple parameters as shows in figures 3-5. Pauwels et al. concluded that the multivariate analysis allows for different classes of drugs to be distinguished. Paull et al. employed a different approach to classify drugs, by use of multiple cell lines that were treated with each alternative drug studied. Each cell line was analyzed for a single parameter of growth inhibition. Paull et al. used the computer program COMPARE to compare the pattern of growth inhibition of each assayed drug over multiple cell lines. Paull et al. concluded that their method allows for different classes of drugs to be distinguished, as shown in Table 2. Because Pauwels et al. (which detects multiple parameters of a single cell line treated with different drugs) did not employ or mention the strategy of Paull et al. (which detects a single parameter of multiple cell lines treated for each drug) it cannot be said that Pauwels et al. teaches away from the method of Paull et al. Because each reference shows advantages to different approaches, and the two different approaches are not conflicting and can both be used to distinguish classes of drugs, it would be obvious to combine the two methods as discussed above.

Double Patenting

12. The provisional rejection of claims 49-57, 60, 61, and 63-65 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 8, 13-15, and 52-64 of copending Application No. 09/310879 is withdrawn in view of the terminal disclaimer filed 30 December 2004.

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13. The provisional rejection of claims 49, 50, 54, 56, 57, 60, 61, and 63-65 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 40-43 and 51 of copending Application No. 09/718685 is withdrawn in view of the terminal disclaimer filed 30 December 2004.

Conclusion

14. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

15. Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of

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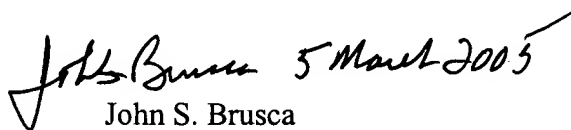
the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center at (800) 786-9199. Any inquiry concerning this communication or earlier communications from the examiner should be directed to John S. Brusca whose telephone number is 571 272-0714. The examiner can normally be reached on M-F 8:30 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, PhD. can be reached on 571 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

 5 March 2005

John S. Brusca

Primary Examiner

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jsb